generic sequence including the specific sequences in parentheses.

35 USC 112(1) Enablement Requirement

The Examiner has rejected claims 1-13 as allegedly in violation of the enablement requirement of 35 USC 112(1). The Examiner has stated that claims 1-13 violate the enablement requirement because claim was is drawn broadly to a first binding element, a second translocation element, and a third therapeutic element. Applicants respectfully traverse this rejection in light of the present amendments.

The enablement requirement of 35 USC §112(2) requires that the specification show the person of ordinary skill in the art how to make and use the invention without requiring undue experimentation. In the present situation, there can be no reasonable assertion made that the specification, combined with the knowledge of the person of ordinary skill in the art, does not show one how to make the invention of the recited claims, particularly in light of the amendments made to claim 1.

Claim 1 has been amended to indicate that the binding element binds a pancreatic acinar cell CCK receptor. The specification, on pages 16 and 17 provides ample disclosure of 6 exemplary binding elements able to bind the CCK receptor. The claim has also been amended to indicate that the second element is a translocation domain derived from a clostridial neurotoxin heavy chain and the third element is a therapeutic element derived from a clostridial neurotoxin light chain.

The precise amino acid sequences of the exemplary CCK receptor-binding elements are given in the specification. Further it would be a matter of routine for the person of skill in the art to make, for example, antibodies directed to the same receptor. To this end, the Court of Appeals for the Federal Circuit has held in *Johns Hopkins University v. Cellpro, Inc.*, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998) that the disclosure of a single hybridoma cell line containing a single monoclonal antibody provided sufficient teaching to enable one to make and use without undue experimentation the genus of all monoclonal antibodies specifically binding to the same antigen. Moreover, the *Johns Hopkins* court quoted and cited with approval its earlier case law illustrating that a

considerable amount of experimentation is permissible to comply with the enablement requirement, if it is merely routine. *Id.* at 1719 (citing *PPG Industries, Inc. v. Guardian Industries, Corp.*, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Moreover, even if a considerable amount of experimentation were necessary, this does not preclude enablement. Both *Johns Hopkins* and *In re Wands* dealt with enablement issues in the field of antibody production; both cases held that the skill in the field is high, that the amount of experimentation necessary is no bar to patentability, and that the techniques employed to raise antibodies, such as the Kohler/Milstein method cited in *Johns Hopkins*, are exceptionally well known in the art.

In the present situation, the CCK receptor sequence is known, as are methods of making ligands thereto (e.g., CCK derivatives and antibodies per *Johns Hopkins*). Moreover, and as acknowledged by the Examiner in the Office Action, the specification enables the skilled worker to make and use the claimed compositions when the translocation and therapeutic elements are derived from a clostridial neurotoxin (i.e., BoNT subtypes A-G and TeNT). Thus, in light of the present disclosure and the state of the art, it would be clear to an undergraduate in biochemistry, much less to those of skill in the art, that it would be a matter of routine to make the claimed compositions based on the instant teachings. For this reason Applicants respectfully request the Examiner to reconsider and withdrawn the rejection of the present claims on the basis of lack of enablement.

35 USC 112(1) Written Description Requirement

The Examiner has also rejected claims 1-13 as lacking written description in the specification. Applicants respectfully traverse this rejection.

The Examiner stated that claims directed to a binding element which binds any pancreatic cell, a "translocation element" and a "therapeutic element" lack sufficient written description because they allegedly define a broad genus which is not sufficiently described by the species disclosed in the specification. Without agreeing with this characterization (Applicants note that the Examiner must overcome a "heavy burden" according to the PTO Final Written Description Guidelines when challenging original claims under the written description requirement), Applicants

issue is now moot in light of the amendments to claim 1, described above. Thus, the binding element now binds to pancreatic acinar cell CCK receptor, and the translocation and therapeutic elements are derived from the heavy and light chains, respectively, of a clostridial neurotoxin; each of these elements is described in the text, and examples of each are given or discussed. Thus the person of skill in the art would recognize that the present inventors were in possession of the claimed invention. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

CONCLUSION

While no fee is thought due in connection with this Statement, if Applicants are in error in this regard kindly use our Deposit Account 01-0885 for the payment of extension or other fees due herewith.

Respectfully submitted,

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VERSION SHOWING MARKED CHANGES

1. (Amended) A composition for the treatment of acute pancreatitis in a mammal comprising, a first element comprising a binding element able to specifically bind a pancreatic acinar cell CCK receptor under physiological conditions, a second element comprising a translocation element derived from a clostridial neurotoxin heavy chain able to facilitate the transfer of a polypeptide across a vesicular membrane, and a third element comprising a therapeutic element derived from a clostridial neurotoxin light chain able, when present in the cytoplasm of a pancreatic cell, to inhibit enzymatic secretion by said pancreatic cell.